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Thrombotic Thrombocytopenic Purpura Associated With HIV and Visceral Kaposi's Sarcoma Treated With Plasmapheresis and Chemotherapy

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We present a case of a patient who is HIV positive and developed both thrombotic thrombocytopenia purpura and visceral Kaposi's sarcoma (KS) with hemorrhage. This case presents a difficult management problem in that the patient's bleeding originated from KS lesions and did not quickly abate with plasmapheresis therapy despite both clinical and laboratory improvement after 2–4 days. Chemotherapy was initiated on day 13 and the patient's condition improved markedly afterward. We believe the addition of chemotherapy to plasmapheresis hastened the improvement of our patient's thrombotic thrombocytopenic purpura (TTP) and KS-related bleeding. Therefore, under similar conditions, we recommend combining plasmapheresis and chemotherapy at the onset of therapy. Am. J. Hematol. 58:148–149, 1998. © 1998 Wiley-Liss, Inc.†

Key words: human immunodeficiency virus; thrombotic thrombocytopenia purpura; Kaposis's sarcoma; chemotherapy; vincristine; doxorubicin

CASE REPORT

R.S. is a 43-year-old African-American male with a diagnosis of HIV with a CD4 count <10/μL. He had known asymptomatic Kaposi's sarcoma (KS) of the nose, hard palate and bronchus and had not received chemotherapy. He presented with a 3-day history of increasing abdominal pain, headache, low-grade fever, and black stools. His admission physical exam was remarkable for mild somnolence, epigastric tenderness, and melena. Peripheral smear was significant for decreased platelets, schistocytes, and fragmented red blood cells. Initial laboratory data revealed a platelet count of 29,000/μL, and an elevated lactate dehydrogenase (LDH) of 868 U/L (normal 100–250 U/L) and normal coagulation studies. Pertinent labs are presented in Table I.

His early hospital course was complicated by hypotension, hematemesis, hypoxemia related to probable pulmonary hemorrhage, spontaneous pneumothorax, and gram-positive bacteremia. Therapy was begun with fluid resuscitation, packed red blood cell transfusions, and broad spectrum antibiotics. A diagnosis of thrombotic thrombocytopenic purpura (TTP) was made due to his clinical presentation, and on day one methylprednisolone at a dose of 200 mg IV and infusions of fresh frozen plasma (FFP) were initiated. Due to the seriousness of his bleeding, a single platelet transfusion was given with each bleeding episode without apparent decline of his clinical status. Esophagogastroduodenoscopy (EGD) revealed the source of his bleeding to be gastric KS lesions. Intralesional epinephrine was injected and the bleeding ceased. Plasmapheresis at 3 liters per day was initiated on day 3. Hematemesis recurred on day 10 despite a decline of the LDH and stabilization of the platelet count at 36,000/μL. Repeat EGD revealed multiple bleeding KS lesions and intralesional epinephrine injection was repeated. As a result of his continued hemorrhage and persistently low platelet counts, chemotherapy directed at KS was started on day 13 consisting of liposomal doxorubicin (Doxil®, 20 mg/m^{2}IV) and vincristine (2.0 mg/IV). He had one final episode of GI bleeding on day 15

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TABLE I. Chronology of Illness*

Day	Hb (12.7–16.6)	Plt (140–400)	Creat (0.7–1.5)	LDH (100–250)	Event
Baseline	10.8	166	0.9	154	
1	5.2	29	1.7	868	GI bleed
2	7.1	32	1.6	1017	FFP
3	6.9	31	2.3	1208	PL Ph
5	8.68	47	2.8	1713	
7	7.75	42	2.6	1405	
10	6.0	36	2.7	835	GI bleed
13	8.86	31	2.2	577	Chemo
15	6.7	28	1.9	497	GI bleed
17	6.6	40	1.7	516	
19	6.32	52	1.8	486	
21	7.97	67	1.6	476	
23	7.76	91	1.6	400	
25	8.1	99	1.3	401	End PL Ph
33	9.28	116	1.6	303	Chemo
120	11.1	133	1.1	238	

*Hb, hemoglobin (gm/dl); plt, platelets/cu mm; creat, creatinine (mg/dl); LDH, lactate dehydrogenase (U/L); GI bleed, gastrointestinal bleed; FFP, fresh frozen plasma; PL Ph, plasmapheresis; Chemo, chemotherapy.

after which no further bleeding occurred despite continued low platelet counts until approximately day 22. Plasmapheresis was discontinued on day 25 when the patient had a platelet count of 99,000 μL and an LDH of 401 U/L. Chemotherapy was continued as an outpatient for a total of six cycles. The patient continues to remain well, 6 months after completing chemotherapy.

DISCUSSION

Kaposi's sarcoma was one of the earliest manifestations of the AIDS epidemic in homosexual men [1]. Epidemiological data later suggested that KS may be sexually transmitted [2], and currently, Human Herpesvirus 8 (HHV8) has been suggested as a possible etiologic agent [3]. HHV8 is found in KS lesions as well as peripheral blood lymphocytes and human semen, further supporting the epidemiologic data suggesting KS is sexually transmitted [3]. TTP is a rare disorder, but in one series, 22% of the patients with TTP had a concurrent HIV or HTLV-1 infection [4], implying an association with retroviral infection. The therapy for HIV-positive patients with TTP is plasmapheresis and similar response rates compared to non-HIV patients are reported, but 1-year survival appears to be worse for HIV patients [5]. Although TTP can occur in the face of malignancy, to date there are no data to suggest that TTP is associated with KS or Herpesvirus 8 infection, and this combination of TTP and KS has not been previously reported in the literature.

This case presents a difficult management problem in that the patient's bleeding originated from KS lesions and did not quickly abate with therapy directed at TTP despite both clinical and laboratory improvement after 2–4 days. In addition, his laboratory abnormalities did not resolve as rapidly as expected. Plasmapheresis generally leads to normalization of the LDH in a median of 5 days (range 2–22), and platelet count in 10 days (range 3–32) [5]. The bleeding event on day 10 prompted us to initiate chemotherapy on day 13 and the patient stopped bleeding after one final event on day 15. The platelet count slowly increased to over 50,000 six days later, and the LDH continued to decrease slowly after chemotherapy. The addition of vincristine to the chemotherapy regimen was important in light of the three case reports demonstrating its effectiveness in refractory or relapsing TTP [6], and its activity in treating KS. We believe the addition of chemotherapy to plasmapheresis hastened the improvement of our patient's TTP and KS related bleeding. Therefore, under similar conditions, we recommend combining plasmapheresis and chemotherapy at the onset of therapy.

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